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Type: Poster Presentation

Final Abstract Number: 48.037
Session: Vaccines & Vaccine Development
Date: Friday, June 15, 2012
Time: 12:45-14:15
Room: Poster & Exhibition Area

Worldwide diversity and distribution of the malaria vaccine candidate MSP1-42: Implications for vaccine design

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Background: Infection with the parasite *Plasmodium falciparum* is associated with the greatest burden of malarial disease worldwide. Despite much investment, an effective malaria vaccine remains elusive. Formation of multivalent subunit vaccines containing *P. falciparum* blood stage antigens known to be a target of the natural human immune response is a current vaccine strategy. The C-terminal fragment of the Merozoite Surface Protein 1 (MSP142) is such a vaccine candidate antigen. However the high levels of diversity in this antigen may restrict vaccine efficacy if not appropriately considered. To provide a global perspective of MSP142 diversity, this study analysed all available MSP142 sequence data together with new data from Papua New Guinea (PNG).

Methods: The MSP142 DNA sequence from 59 isolates obtained from two parasite populations in PNG were compared to MSP142 sequence data collated from online databases and published literature. Genetic diversity, population structure and natural selection were measured.

Results: A total of 267 MSP142 sequences from seven malaria endemic countries were analysed. Of the two MSP142 allele families, the majority of sequences (88%) belonged to the MAD20 allele family, and the remainder to the K1 family. K1 sequences consisted of five non-synonymous haplotypes which occurred at varying frequencies in three countries; Iran, Thailand and PNG. In the MAD20 sequences 74 non-synonymous haplotypes were identified. The distribution of MAD20 haplotypes was geographically influenced, and many haplotypes were found in only a single country population. Of the haplotypes currently employed in vaccine trials, 3D7 was absent or found at low frequencies in country populations, while FVO/K1 was restricted to the Asia-Pacific. The minimal number of haplotypes required to achieve 50% coverage worldwide was eight. Restricting this analysis to the 12 polymorphisms in MSP142 that show evidence of balancing selection resulted in 56% coverage on inclusion of the three most common haplotypes.

Conclusion: This investigation reiterates the call for genetic diversity to be considered in malaria subunit vaccine design, as careful consideration of the population genetics might provide a diversity-covering approach.

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Hospital based surveillance of rotavirus gastroenteritis in children <5 years of age in Lebanon

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Background: Rotavirus (RV) is the single most common cause of severe gastroenteritis (GE) in children aged <5 years worldwide. Data on the burden and epidemiology of RV disease in Lebanon is limited. Therefore, this study aimed to determine the attributable fraction (AF) of RV as the etiologic agent of GE, RV strain distribution and seasonality of RVGE in children aged <5 years in Lebanon.

Methods: This multicenter, hospital-based surveillance conducted between May 2007 and May 2008, enrolled children <5 years hospitalized with GE episodes. Stool samples were tested

for the presence of RV by enzyme immuno assay (EIA). RV positive samples were genotyped by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). Seasonality of RVGE cases was recorded during the study period. Severity of the RVGE episodes was measured using the Vesikari scale, where a score of ≥11 was considered severe.

Results: Of the 534 children enrolled in this study, 491 (91.9%) were included in the final analysis in the according-to-protocol cohort; 27.7% (136/491) of subjects were RV positive, 71.5% (351/491) were RV negative and 0.8% (4/491) had unknown RV status. Of the RV positive subjects, 75% (102/136) of cases were seen in children <2 years of age. Although RVGE cases occurred throughout the year, the peak season was observed between December 2007 and March 2008 (65.4%; 89/136). Severe GE cases observed before hospitalization was 79.4% (108/136) in RV positive and 76.1% (267/351) in RV negative subjects (p = 0.44). G4 (36.9%) and P[8]WT (77.7%) were the most common RV types detected among RV positive samples that were genotyped (N = 130).

Conclusion: The data generated from this first burden of disease study in Lebanon showed that the AF of Rotavirus in children <5 years of age corresponded to 27.7% of hospitalized GE. Most of the RV cases (75%) were in children aged <2 years. These baseline epidemiology data might guide policy makers in initiating nationwide public health strategies, including vaccination to reduce the RV disease burden in Lebanese children <5 years of age.

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Antifungal susceptibility of *Cryptococcus neoformans* and clinical correlation

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Background: The incidence of cryptococcosis has increased over the past 30 years as the result of the AIDS pandemia and immunossuppresive treatments. It has been reported the presence of resistant strains *in vitro* to antifungal drugs. The proposed correlation between minimum inhibitory concentration (MIC) of the isolated *C. neoformans* strains and the clinical course is still controversial.

The aim of this study was to determine the correlation between the MICs of fluconazole and amphotericin B for *C. neoformans* and the clinical course of cryptococcal meningitis in AIDS patients.

Methods: We performed a prospective study between 2009 y 2010 in the Infectious Diseases Hospital (Montevideo, Uruguay) that enrolled 33 patients that met the inclusion criteria (adults, HIV positive, cryptococcal meningitis confirmed by isolation of the strain of cerebroespinal fluid). The study was approved by the ethics committee of the participating institution.

The identification of the strains was performed by phenotipic studies. All of isolates belongued to *C. neoformans var neoformans*. Susceptibility to fluconazol and amphotericin B determined by the CLSI broth microdilution metodology.

Results: Sambple characteristics: of the 33 patients 21 were male, all had CD4 ≤ 200/mm3, 9 had biochemical and cytological study of cerebrospinal fluid tests. 24 wrere already had a diagnose of AIDS and were no receiving HAART. 4 patients died during hospitalization for reasons related to cryptococcal meningitis. The study of antifungal susceptibility showed MICs of o,25 - 4υg /ml to fluconazole and 0,03-0,5ug/ml in the amphotericin B. Therefore, no strain showed in vitro resistance to any of the antifungal agent tested and futhermore, no established relation between MICs and clinical outcome.

Conclusion: Determining the susceptibility to antifungal shows no strains of *C. neoformans* resistant or clinical problems related to resistance. No relationship was found between clinical outcome and antifungal MICs and all the strains in vitro since all strains were susceptible. Severe immune deterioration due to the absence to HAART seems to be the most important determinant for the development of the life threatening cryptococcosis in this population.

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The predictive rule for the management of hospital-acquired pneumonia in adults by the Japanese Respiratory Society, I-ROAD, could correctly estimate the severity of Pneumcystis Pneumonia without human immunodeficiency virus infection

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Background: Non-HIV Pneumocystis pneumonia (PCP) could occur in immunosupressed patients having malignancy or on immunosuppressive agents. A-DROP system by the Japanese Respiratory Society (JRS), CURB-65 score by British Respiratory Society (BTS) and the Pneumonia Severity Index (PSI) by the Infectious Disease Society of America (IDSA) are widely used in classifying patients with CAP in Japan. Another predictive rule, I-ROAD, is used for hospital associated pneumonia (HAP) in Japan. We previously reported that I-ROAD could evaluate correctly the severity of CAP as well. For the purpose of evaluating how correctly the I-ROAD could reflect the severity of non-HIV PCP, we retrospectively analyzed all the non-HIV PCP patients.

Methods: We reviewed all non-HIV PCP patients admitted to our department from 2009 to 2011. A total of 23 non-HIV PCP patients were enrolled in this study. Patients' characteristics, the severities of pneumonia, outcomes and the accuracy of predictive rules in each guideline were evaluated.

Results: A total of 23 non-HIV PCP patients were enrolled in this study. The patients were 13 males and 10 females. Fourteen were cured and 9 were dead. Based on A-DROP, 20 of the 23 (87%) patients were classified as mild or moderate. Sixteen of 20 (80%) developed respiratory failure and 8 of the 16 (50%) died. Based on CURB-65, 21 of 23 patients (91.3%) were evaluated as mild or moderate. Seventeen of the 21 (81%) developed respiratory failure and 9 of the 17 (52.9%) died. Based on PSI, 8 of 23 patients (34.8%) were evaluated as mild or moderate. Four of the 8 (50%) developed respiratory failure and 1 of the 8 (12.5%) died. However, based on I-